

DRUG-INDUCED ACUTE KIDNEY INJURY

By

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إِنَّا عَرَضْنَا الْأَمَانَةَ عَلَى السَّمَاوَاتِ وَالْأَرْضِ وَالْجِبَالِ
فَأَبَيْنَ أَنْ يَحْمِلْنَهَا وَأَشْفَقْنَ مِنْهَا وَحَمَلَهَا الْإِنْسَانُ إِنَّهُ كَانَ
ظَلُومًا جَهُولًا (72) سورة الأحزاب



Introduction

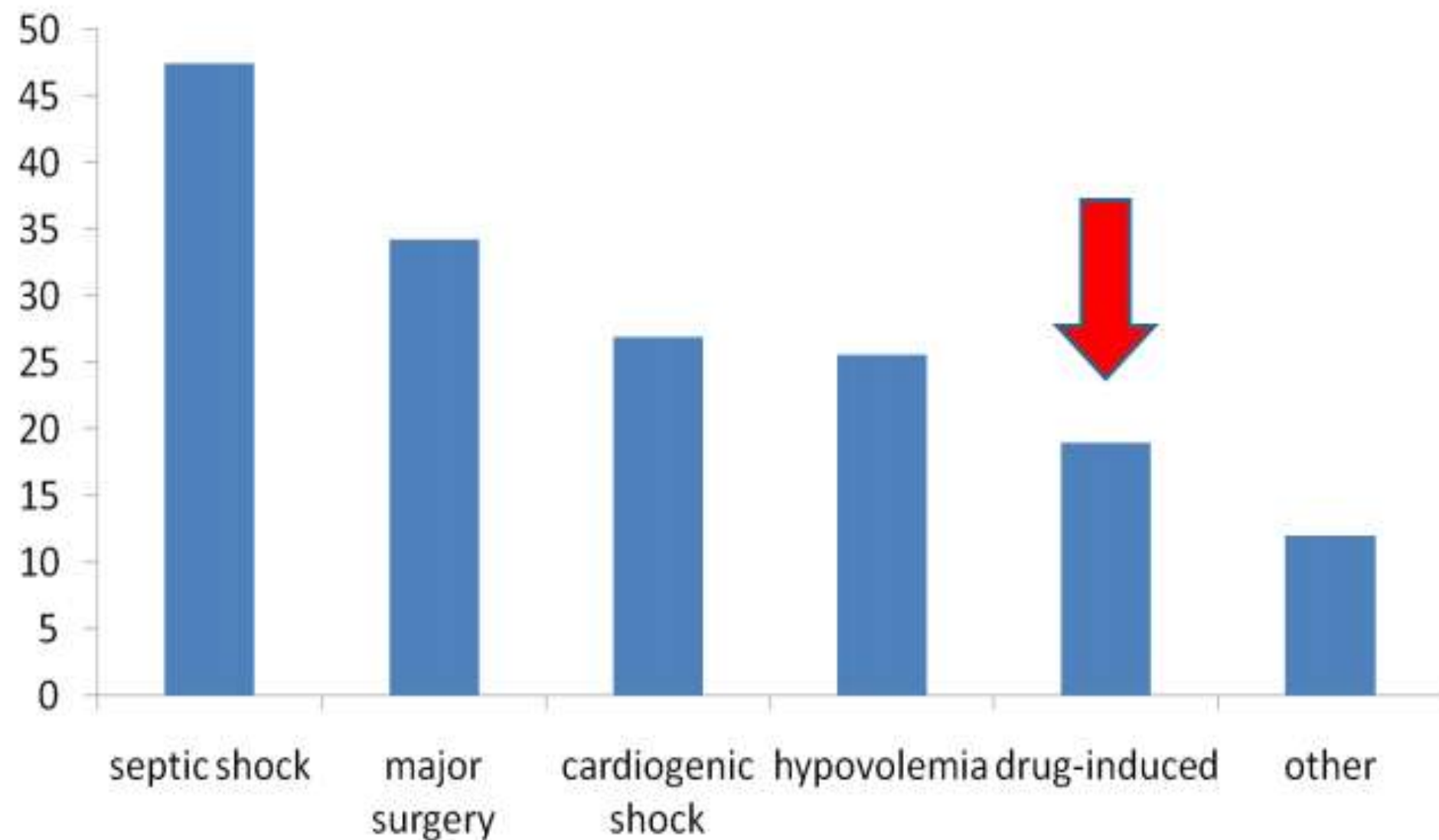


- Drug-induced kidney failure is a major adverse event associated with multiple medication classes
- Medications as diverse as OTC analgesics (ibuprofen, acetaminophen), antibiotics and chemotherapy agents can cause kidney damage
- Medication use accounts for 2% of hospital admissions for acute renal failure and up to 15% of admissions into intensive care

Causes of ARF in H.patients

- Up to 16% of patients with baseline normal renal function who experience renal failure within the hospital setting have medication-induced renal failure

Contributing factors of AKI in ICU



Why kidney is easily exposed to Toxin and Drug

- Blood flow $1/3$ of cardiac output
- High energy demand
- Water reabsorption, increase Concentration
- Tubular reabsorption of drug

Drug induced AKI share common risk factors



Dehydration

Old Age

Pre-existing
kidney disease



Concomitant
nephrotoxic

Heart failure
Liver disease
hypoalbuminemia

Clinical presentations



- Patients who experience acute-onset renal failure often complain of increased shortness of breath, ankle swelling and weight gain
- Drug-induced renal disease can mimic renal disease from other causes, such as autoimmune disease and infection
- A thorough physical examination and medical history should be performed

Contd.



- A thorough and accurate review of all medications, including all prescription, over-the-counter and herbal medications
- Importance of dose and duration of exposure
- rule out all other causes of kidney failure

Clinical feature of patient with AIN

<i>Feature</i>	<i>Percent</i>
Arthralgia	45
Fever	36
Skin rash	22
Eosinophilia	35
Microhematuria	67
Gross hematuria	5
Leukocyturia	82
Non-nephrotic proteinuria	93

TABLE 1. DRUG CLASSES ASSOCIATED WITH RENAL FAILURE/DYSFUNCTION

Antibiotics

Analgesics

Anticonvulsants

Antivirals

Amphotericin B

Antineoplastics

Antihypertensives

Drugs of abuse

Diagnostic agents

Herbal supplements

HMG-CoA reductase inhibitors

Immune globulin

H₂-antagonists

Lithium

Proton pump inhibitors

Others

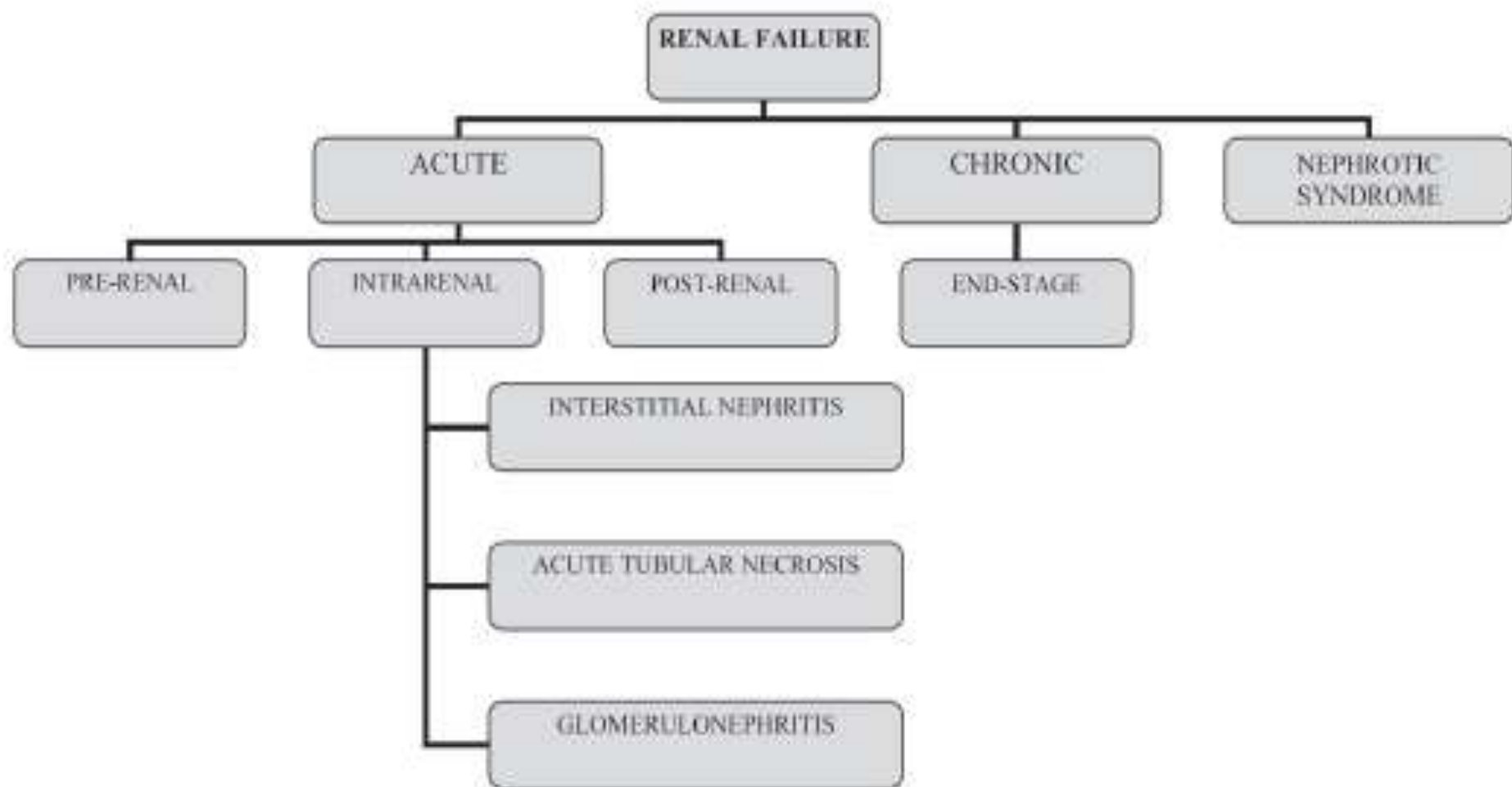


FIGURE 3. CLASSIFICATION OF DRUG-INDUCED RENAL FAILURE

Based on time frame (acute or chronic). Sub-classification of acute renal failure based on cause (pre-renal, intrarenal or post-renal). Nephrotic syndrome occurs with glomerular damage and the excessive loss of protein in the urine.

Pre-renal causes

□ **Vasoconstriction**

1. Amphotericin, noradrenaline and immunosuppressive agents such as tacrolimus and ciclosporin
2. Contrast agents
3. Iodinated contrast media, in particular, have been shown to inhibit the synthesis of nitric oxide in renal artery smooth muscle

□ **Diuretics**

Intrarenal failure

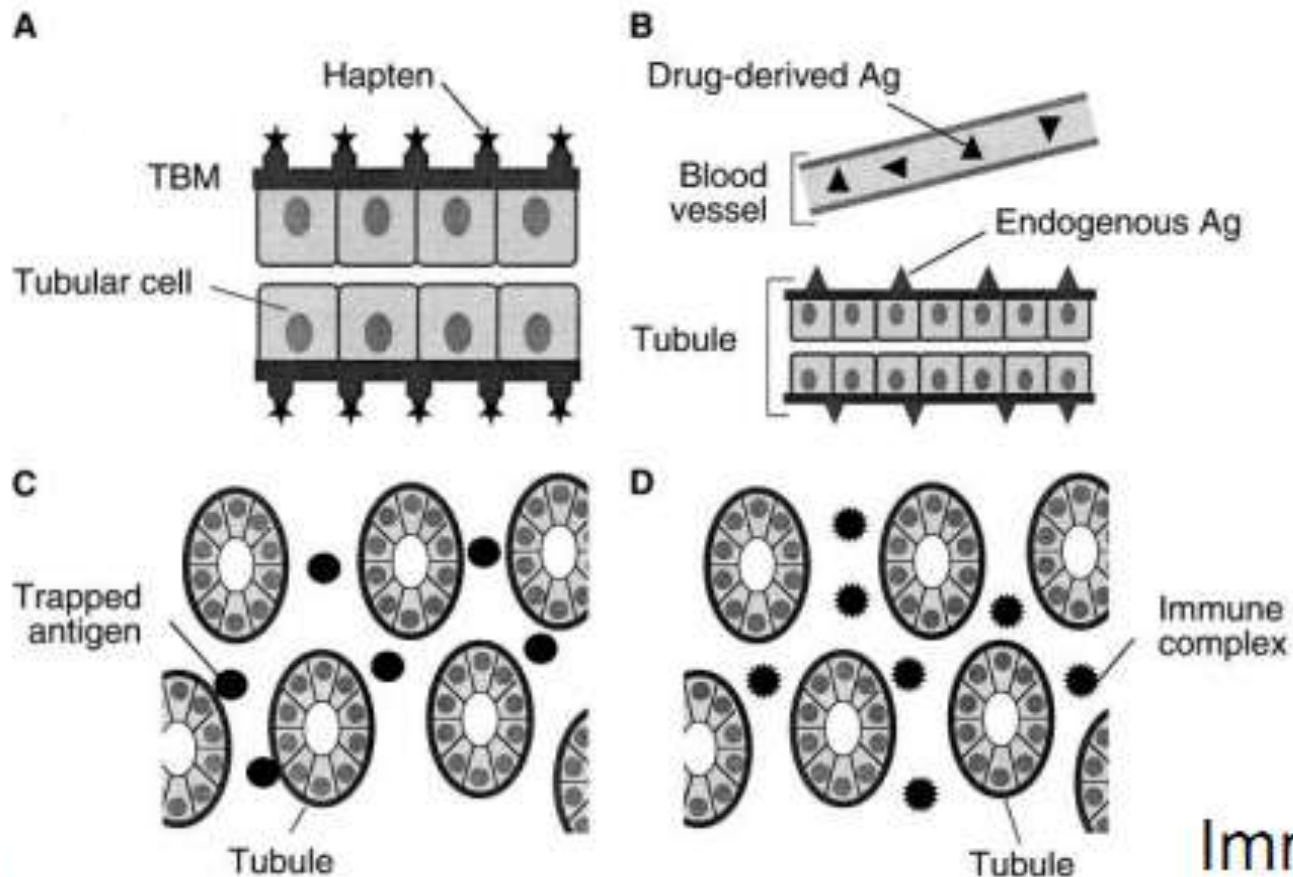
- Some medications can cause a localized allergic reaction affecting the glomerulus (glomerulonephritis)
 1. penicillins, sulphonamides, rifampicin, cephalosporins and ciprofloxacin, AGs
 2. Phenytoin
 3. PPIs
 4. NSAIDs

Contd.

- Affecting surrounding renal tissue (**Interstitial nephritis**)
- More severe event occurs if the drug has a direct toxic effect on the tubules within the nephron (**Acute tubular necrosis or ATN**) eg., AGs.
- ATN can develop within hours to days from initial exposure

Hapten

Antigen



Trapped
antigen

Immune
complex

Pathogenesis

Osmotic nephrosis

- high doses of mannitol, immunoglobulins, dextrans and starch are nephrotoxic
- Direct effect on glomerular filtration
- or the uptake of these large molecules by pinocytosis into the proximal tubule
- sucrose-based IVIG: The renal failure began from 1 to 10 days after therapy

Nephrotic syndrome



- ❑ Drugs : NSAIDs, penicillamine and gold
- ❑ damage the glomerulus and alter the ability of the glomerulus to prevent protein from being filtered
- ❑ Stopping the drug may resolve the damage to the glomerulus

Post-renal failure

- usually results from a mechanical barrier to moving urine from the collecting tubules into the bladder
- Mechanical obstruction :
 - ▣ Drugs that precipitate in the kidney (acyclovir, ganciclovir)
 - ▣ Co-trimoxazole

ANTIBIOTICS

- ❑ AIN is a hypersensitivity or allergic reaction to the drug
- ❑ Up to 71% of all cases of acute interstitial nephritis (AIN) are drug-induced
- ❑ The most common antibiotic classes associated with AIN are penicillins/cephalosporins and sulfonamides, ciprofloxacin and Rifampin

Contd.

- Aminoglycosides (tobramycin, gentamicin, amikacin) and amphotericin B can cause ATN
- Risk of aminoglycoside toxicity is associated with increased dose, duration of therapy, dehydration and concurrent use of nephrotoxic drugs, such as NSAIDs
- Amphotericin B renal toxicity is related to cumulative dose, concurrent use of nephrotoxic drugs, baseline abnormal creatinine and concurrent use of diuretics
- 80% of patients receiving amphotericin B experiencing some decrease of renal function
- Saline hydration can decrease the toxicity

ANTIVIRALS

- ❑ Cidofovir, foscarnet, acyclovir and interferons can cause ATN
- ❑ Acyclovir can precipitate within the renal tubules

NSAIDs

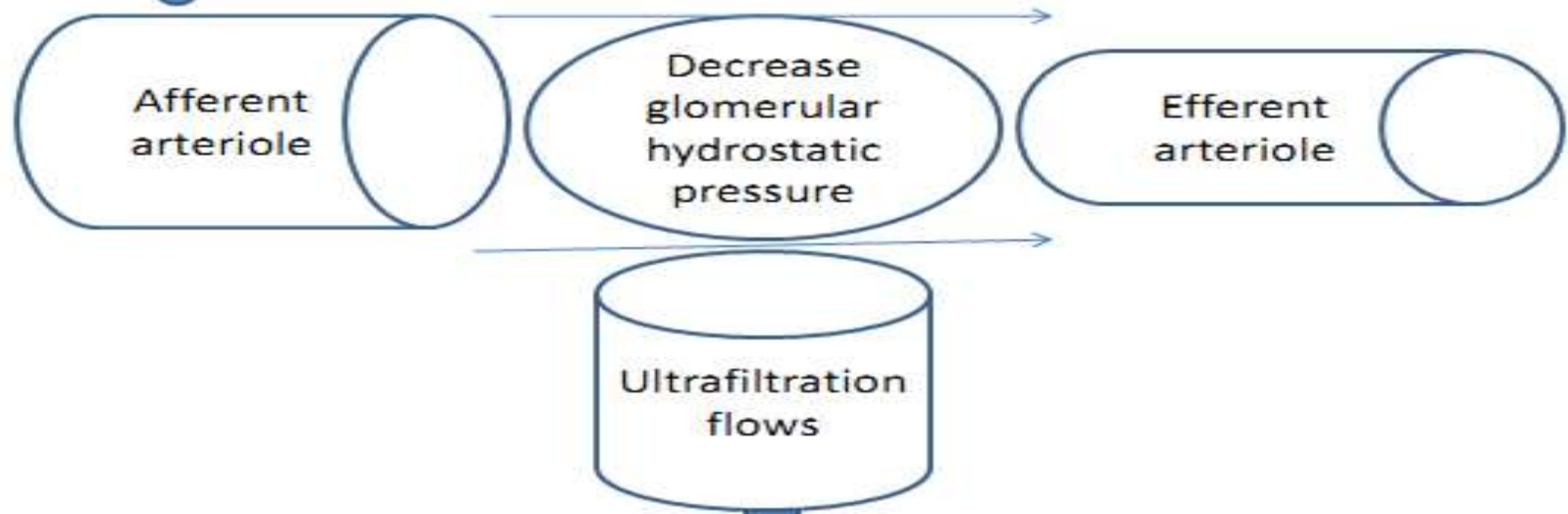


- Patients who experience ARF with NSAIDs have underlying risk factors
- 1-5 % of all end-stage renal disease (ESRD) patients have analgesic-associated nephropathy
- Risk factors for this nephropathy include gender (women>men), age (>50 years old) and prolonged use of the analgesic

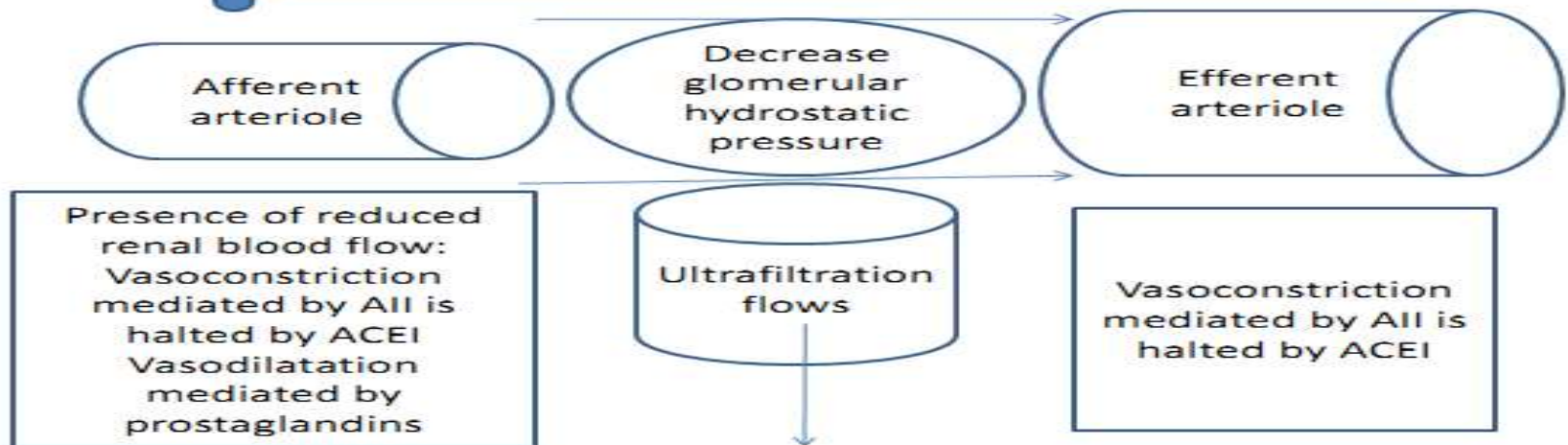
NSAIDs

- Selective cyclooxygenase (COX-2) inhibitors cause similar renal dysfunction
- COX-2 exists as a constitutive enzyme in the thick part of the ascending loop of Henle and in the renal medulla
- COX-2 causes natriuresis and diuresis
- Inhibition of COX-2 by selective COX-2 inhibitors, such as celecoxib and rofecoxib causes renal dysfunction
- particularly in patients who are volume-depleted or haemodynamically unstable

Maintaining of GFR



NSAIDs, ACEI/ARB



Decrease glomerular filtration

CHEMOTHERAPY-INDUCED RENAL INJURY



- Nephrotoxicity is the major dose-limiting toxicity for cisplatin
- Both acute and late-onset toxicities occur
- Aggressive replacement of magnesium (lost when the proximal tubule is damaged), saline hydration or mannitol infusion

Contd.

- High dose methotrexate : postrenal obstruction by precipitating in the tubules of the nephron and direct toxicity
- Tumour lysis syndrome.

IMMUNOSUPPRESSANT



- Cyclosporine and tacrolimus
- Acute, dose-dependent reduction in renal blood flow and chronic structural changes in the kidney

STATINS



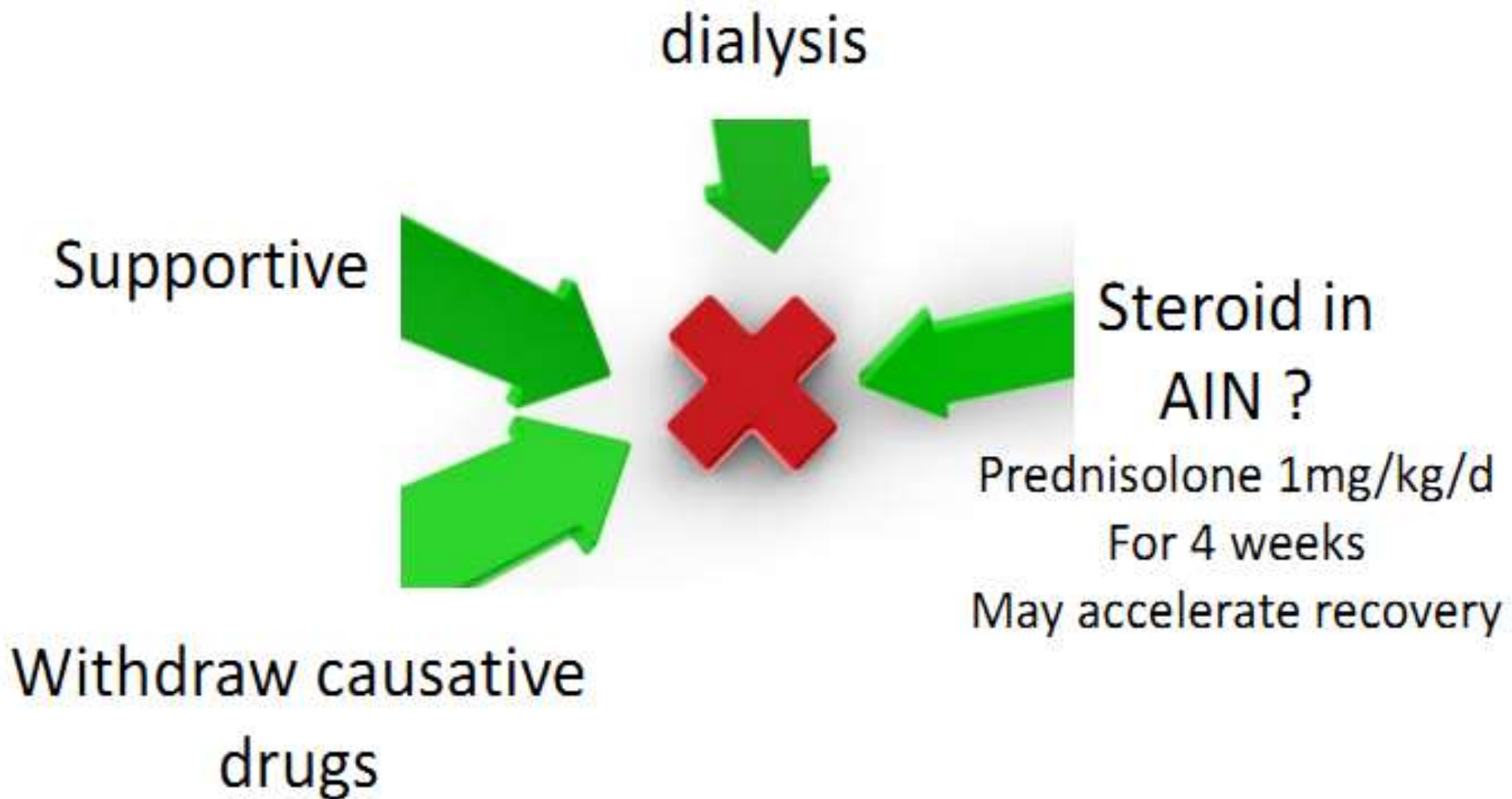
- ❑ Rare but serious cases of rhabdomyolysis
- ❑ Acute tubular necrosis
- ❑ Muscle pain, dark urine, electrolyte abnormalities and renal failure

DRUGS OF ABUSE



- ❑ Cocaine and heroin
- ❑ Cocaine use can cause renal artery thrombosis (clotting), severe hypertension and interstitial nephritis
- ❑ Long-term cocaine use can lead to chronic renal failure
- ❑ Long-term tobacco use also increases the risk of kidney cancer???

Summary in treatment of drug induced AKI



Conclusion



- ❑ Many drugs cause AKI
- ❑ Age (particularly over 65 years), pre-existing renal impairment, comorbidities such as diabetes mellitus, heart failure, liver cirrhosis and hypovolaemia are risk factors.
- ❑ Addressing potential risk factors
- ❑ Understanding of the mechanisms of nephrotoxicity involved.

LIFE is the most difficult EXAM.

Many people fail because they try to copy others -
Not realising that everyone has a different question
paper!



